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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,005	09/11/2000	Erich Wanker	V0179/7001	1379

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/485,005	WANKER ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-20 and 27-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *13-16 and 31-41* is/are allowed.

6)☒ Claim(s) *1-5,7-12,17-20 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2006 has been entered.

Restriction Election

2. Applicant's amendment and response filed November 14, 2005 is acknowledged and has been entered. Claims 1, 4, 7, 12, 13, 15-20, and 28-30 have been amended. Claim 6 has been cancelled. Claims 33-41 have been added. Accordingly, claims 1-5, 7-20, and 27-41 are pending and are under examination.

Withdrawn Rejections

3. All rejections not reiterated herein, have been withdrawn

4. The rejection of claim 6 is now moot in light of Applicant's cancellation of the claim.

5. In light of Applicant's amendment, the rejection of claims 1-5, 8-12, 18-20, and 27 under 35 U.S.C. 102(a) as being anticipated by Kalchman et al. (WO 97/18825), is hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 7-12, 17-20, and 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "low capacity" in claim 1 is a relative term which renders the claim indefinite. The phrase "low capacity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5, 7-12, 17-20, and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Notario et al. (Changes in the membrane proteins of blood cells in the course of embryonal megaloerythropoiesis in relation to hemoglobin maturation) Archivio per le scienze mediche, 135 (1): 1-8 (1978 Jan-Mar) Abstract) in view of Mueller (US Patent 4,094,775) or Gokcen (US Patent 6,428,785) and in further view of Kalchman et al. (WO 97/18825).

Notario et al. teach contacting a sample material having protein aggregates from membrane proteins after solubilization by urea or detergent, sodium dodecyl sulphate (SDS), with a cellulose acetate filter. Protein aggregates on the cellulose acetate filter are subjected to hemoglobin electrophoresis for detection of membrane proteins (see Abstract).

Notario et al. is silent in teaching that the cellulose acetate filter is used in filtering the sample to retain and capture the urea or detergent insoluble protein aggregates for subsequent detection.

Mueller discloses that cellulose acetate membrane filters are used in filtration methods for capturing or retaining (preventing passage of) very large protein molecules and cellular constituents (see column 4, lines 27-37).

Gokcen discloses that cellulose acetate and polysulfone membrane filters are low protein binding filter membranes used in filtration methods for capturing or retaining insoluble protein aggregates (see column 10, lines 23-28).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have captured and retained the urea insoluble protein aggregates in the cellulose acetate membrane filter as taught by Notario in a filtration process as taught by Mueller or Gokcen, because both of Mueller and Gokcen specifically provided that cellulose acetate membranes are known for their low adsorption or protein binding capability and are conventionally and advantageously used for separating, capturing, and isolating large insoluble protein molecules in membrane filters.

Notario, Mueller, and Gokcen differ from the claimed invention in failing to teach identifying the captured protein aggregates or myeloid-like fibrils that are retained in the low adsorption filter.

Kalchman et al. provide that the interaction between HD proteins and HIP1 is influenced by the number of polyglutamine repeats and that expanded polyglutamine tracts aggregate into large irregularly shaped deposits in brains of Huntington disease (see pages 1, 6, and 7). Kalchman et al. provides that individuals suffering from Huntington's disease have polyglutamine expansions of at least 35 glutamines, at least

41 glutamines, at least 48 glutamines, or at least 51 glutamines, (36 or greater glutamines) (see page 2). Kalchman et al. also found that HIP1 protein is insoluble to treatment with Triton X-100 (see Examples 7 and 8). In practice, proteins from tissues and cells of human and other mammals are solubilized with detergent, and spotted or dotted (electroblotted) on SDS-PAGE mini-gels so as to capture HIP1 and huntingtin proteins for detection. Immunoreactivity is determined using antibodies against HIP1 and Huntingtin and visualized in chemiluminescent ECL solution.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have substituted cellulose membrane filters as taught by Notario as modified by Mueller or Gokcen, into the filtering device used in the method of Kalchman in capturing and isolating the large insoluble proteins or amyloid-like fibrils such as HIP1 as identified by Kalchman to be detergent insoluble protein, because Mueller and Gokcen specifically provided that cellulose acetate membranes are known and conventionally used as filters in filtering, capturing, and retaining material having large insoluble protein molecules in their membrane and are recognized for their advantage of having low adsorption or protein binding capability, which render them useful in filtration and isolation methods and systems such as that taught by Kalchman, in identifying specific insoluble and large protein aggregates or amyloid-like fibrils that are would have been retained in the membrane filter.

Response to Arguments

9. Applicant's arguments with respect to claims 1-5, 7-12, 17-20, and 27-30, filed on November 14, 2005, have been considered but are moot in view of the new grounds of rejection.

Allowable Subject Matter

10. Claims 13-16 and 31-41 are clear of the prior art of record. The prior art of record fails to teach or fairly suggest filtering and capturing detergent- or urea-insoluble amyloid-like fibrils or protein aggregates on low capacity protein adsorption filter and detecting the presence or concentration thereof, wherein the captured amyloid-like fibril or protein aggregate is a fusion protein comprising 1) a polypeptide that enhances solubility or prevents aggregation of the fusion protein; 2) an amyloidogenic polypeptide that self assembles into amyloid-like fibrils or protein aggregates when released from the fusion protein; and 3) a cleavable site that separates 1) and 2) of the fusion protein; and wherein the fusion protein is further incubated with a suspected inhibitor of amyloid-like fibrils and protein aggregate formation, and simultaneously or concurrently, with a compound that induces cleavage at the cleavage site. The object of using low capacity protein adsorption filter is to capture only detergent- and urea- insoluble amyloid-like fibrils and protein aggregates in the filter membrane for detection, and to ensure exclusion of solubilized fibrils and proteins are filtered into solution.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571)

272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday from 7:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
April 7, 2006